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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/043,440	01/10/2002	Costas D. Maranas	P05468US1	1336
27407	7590	12/27/2007	EXAMINER	
MCKEE, VOORHEES & SEASE, P.L.C. ATTN: PENNSYLVANIA STATE UNIVERSITY 801 GRAND AVENUE, SUITE 3200 DES MOINES, IA 50309-2721			CLOW, LORI A	
ART UNIT		PAPER NUMBER		
		1631		
MAIL DATE		DELIVERY MODE		
12/27/2007		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)
	10/043,440	MARANAS ET AL.
	Examiner	Art Unit
	Lori A. Clow, Ph.D.	1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 09 October 2007.
 2a) This action is FINAL. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-8, 10-16, 19-27 and 30-33 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 1-8, 10-16, 19-27, and 30-33 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
 3) Information Disclosure Statement(s) (PTO/SB/08)
 Paper No(s)/Mail Date _____
- 4) Interview Summary (PTO-413)
 Paper No(s)/Mail Date. _____.
 5) Notice of Informal Patent Application
 6) Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Applicants' response, filed 9 October 2007, has been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-8, 10-16, 19-27, and 30-33 are currently pending. Claims 9, 17, 18, 28, and 29 have been cancelled.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8, 10-16, 19-27, and 30-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 6, 19, 23, 30, and 33 recite in each preamble "modeling cellular metabolism of an organism" but the steps/instructions of the claims fail to recite any relationship of an FBA

model to an organism. As it is unclear what relationship is intended between the preamble of each claim and the actual steps/limitations recited, the claims are indefinite. Claims 2-5, 7, 8, 10-16, 20-22, 24-27, 31, and 32 depend from one of claims 1, 6, 19, 23, 30, and 33 and fail to overcome the indefiniteness of the parent claims, and are therefore also indefinite.

Response to Applicant's Arguments

1. Applicant argues that the claims are "sufficiently clear to satisfy the requirements of the second paragraph of 112". Applicant submits that the claims have been amended to "more explicitly recite that relationship between the preamble and the claimed FBA model".

This is not persuasive. For example, claim 1 has been amended to recite, "flux balance analysis model of cellular metabolism of the organism". However, it remains unclear as to what "constructing a flux balance analysis model" and "applying logic constraints...to the flux balance analysis model to produce an altered flux balance model" has to do with improving predictive capabilities of a flux balance model of cellular metabolism. It is unclear what relationship exists between the method steps. What does construction of a model have to do with improving predictive capabilities? Clarification through clearer claim language is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an

international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-8, 12-15, 19, 22, 23, 25-27, 30, 31, and 33 remain rejected under 35 U.S.C. 102(e) as being anticipated by PALSSON (US 2002/0012939), for the reasons set forth in the previous Office Action and re-iterated below. The additional statements have been added as necessitated by amendment.

PALSSON teaches modeling cellular metabolism utilizing stoichiometric mass balances (para's 31-34), and teaches application of constraints (para's 40-45) which result in a restricted (tightened) model (para 40), wherein the constraints may be applied to change a flux boundary to thereby produce an improved model (para 43); PALSSON also teaches the construction of a matrix (para 18), thereby anticipating claims 1, 6, 19, 23, and 33. These constraints may include those which are required to meet maintenance requirements with regard to energy (kinetic) requirements; i.e. prevent violation of a kinetic barrier/boundary (para 43) or may include "connectivity" constraints; i.e. constraints including information with regard to connections between fluxes inside and outside the cell (para 45); thereby anticipating claims 2-3, 7, 21, and 25. PALSSON specifically teaches that by adjusting constraints, it is possible to optimize the flux distribution through the metabolic network (para's 47 and 57-59); i.e. to improve/optimize the predictive capabilities of the model as it applies to the metabolic network. The constraints are those which relate reaction fluxes and metabolic concentrations of analytes in a network (para 45), therefore claim 8 is anticipated. PALSSON also teaches use of mixed integer linear programming (para's 44-46), use of differential DNA microarray data (para 60), and solving for desired metabolic outcomes (para 41 and Examples, pp. 5-6), thereby anticipating claims 4-5,

14-15, 19, 22, 26-27, and 30-31. PAULSSON teaches determination of minimal media for growth of an organism, which is inherently a teaching for identifying a minimal set of metabolic reactions (para 61), and teaches determining the effect of "deletions" in his model (Example 2, p. 6), which is also inherently a teaching for calculating a minimal set of reactions necessary for growth, which teachings anticipate claims 12-13.

Response to Applicant's Arguments

1. Applicant argues that "claim 8 is a dependent to claim 6. Therefore, any alleged 'definition' purported to be found in this claim should not form the basis of a rejection to independent claims 1, 19, 23, 30 or 33. Further, the recited element of claim 8 further limits the base claim and, although it includes all of claim 6's elements, it does not define the term 'logic constraints' as claimed. Rather, the specification defines the meaning of claim terms".

This is not persuasive. Firstly, it is pointed out that the specification defines "logic constraints" to be constraints taken from kinetic information, regulatory information and/or DNA microarray experimental data information (page 1) and that "preferably constraints are represented by binary values" (page 4). The specification also teaches that "the key idea we propose to explore is to ensure, by using logic relations, that when, in response to environmental changes, the metabolic network shifts from one steady-state to another, up or down changes in metabolic concentrations are consistent with up or down changes in reaction fluxes". Therefore, the specification offers several "definitions" of logic constraints, of which one definition is consistent with the meaning in claim 8. Therefore, the "logic constraints" of the independent claims, such as claims 1, 6, 19, 23, 30, and 33 can include all definitions from the specification

as originally filed, as the claims do not limit the definition to a particular embodiment. Further, PALSSON teaches using constraints which include at least regulatory constraints, as was pointed out previously at paragraphs [0054] and [0059]. Therefore, the rejection is maintained.

2. Applicant argues that PALSSON does not describe applying logic constraints to produce an altered flux balance analysis model.

This is not persuasive. As stated above, PALSSON teaches that constraints may be applied to change a flux boundary to thereby produce an improved model, thus teaching applying constraints to produce an altered model. Therefore, the claims remain rejected.

Conclusion

No claims are allowed.

The outstanding rejection under 35 USC 112, 1st paragraph has been withdrawn in view of the amendments to the claims removing the language "subsets".

The outstanding rejections under 35 USC 112, 2nd paragraph with respect to claims 16 and 32 ("based on" language) has been withdrawn in view of the claim amendments.

The outstanding rejections under 35 USC 112, 2nd paragraph over claim 30 has been withdrawn in view of the amendment to the claim.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central Fax Center Number is (571)-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

LORI A. CLOW, PH.D.
PRIMARY EXAMINER



December 21, 2007
Art Unit 1631